

## Main results obtained in a series of animal experiments for the assessment of the organism's responses to metallic nanoparticles (self-review).

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Nanoparticles (NPs) of Fe<sub>3</sub>O<sub>4</sub> were produced by a chemical technique and nanoparticles of Ag, Au, CuO, NiO, Mn<sub>3</sub>O<sub>4</sub>, PbO, ZnO, TiO<sub>2</sub>, SiO<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub> - by laser ablation. In some experiments, we compared particles of a given chemical composition having different diameters, while in others – equidimensional NPs of different metals or metal oxides (Me-NPs).

We used two experimental models: (a) a single intra-tracheal instillation of Me-NPs 24 h before the bronchoalveolar lavage to obtain a fluid for cytological and biochemical assessment; (b) repeated intra-peritoneal injections during 6-7 weeks in non-lethal doses to assess the thus induced subchronic intoxication by a lot of functional, biochemical and morphological indices. Besides, we carried out long-term inhalation experiments with NPs of Fe<sub>2</sub>O<sub>3</sub>, SiO<sub>2</sub> and NiO.

We demonstrated that NPs are much more noxious as compared with their fine micrometric or even submicron counterparts and are usually the more toxic the smaller their dimensions *within* the nano-scale range. However, for the RES-rich organs this dependence is not so unique due to intricate and contra-directional influences of the Me-NP's size on toxicodynamics and toxicokinetics. We found also that toxicity of Me-NPs strongly depends on their chemical nature, solubility and specific mechanisms of action characteristic of a given metal in any chemical form. Solubilization of Me-NPs in biological milieus plays an important part in their toxicokinetics which can prevail over that of the physiological mechanisms controlling their distribution, retention and elimination.

On the other hand, thanks to the high activity of these mechanisms, the organism is not defenseless against the impact of Me-NPs. As the protective measure, the toxicity and even genotoxicity of Me-NPs can be significantly attenuated by adequately composed combinations of some bioactive agents in innocuous doses.